

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: P. A. Billing-Medel, *et al.*

Serial No.: 09/052,855

Filed: March 31, 1998

For: REAGENTS AND METHODS
USEFUL FOR DETECTING
DISEASES OF THE
GASTROINTESTINAL TRACT

Examiner: N. Johnson

Group Art Unit: 1642

Case No.: 6064.US.P1

Date: September 14, 2000

**CERTIFICATE OF MAILING (37 CFR
1.8 (a))**

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the:

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Date of Deposit: October 11, 2000

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Wanda E. Smith Date

**DECLARATION OF
PAULA N. FRIEDMAN Ph.D.**

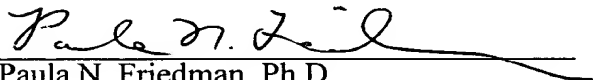
Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

1. I am one skilled in the art of cancer diagnostics. I have a Ph.D. in Molecular Biology from Columbia University as well as an M.A. and a M. Phil. in Molecular Biology also from Columbia University. I further have a B.A. in Biology from Dartmouth College.
2. I was a Postdoctoral Fellow in the Laboratory of Dr. Clay Siegall at the Pharmaceutical Research Institute Bristol-Myers Squibb and an Assistant Pharmacologist, Dept. of Clinical Immunology & Biol. Therapy at the MD Anderson Cancer Center.
3. I have nine years of research and development experience in the cancer diagnostic industry. Much of my work has involved the discovery and validation of novel cancer markers to improve the accuracy of diagnosing the onset of cancer. In fact, I am a named inventor of several U.S. Patents, all of which are related to the field of cancer diagnostics.
4. I also have authored numerous journal articles relating to cancer pathology, detection, and metastasis (see Attachment I).

5. I am one of the named inventors of the aforementioned application.
6. I have read and am familiar with the Patent Office Action dated June 20, 2000 and utility rejection under 35 U.S.C. 101 applied against the present application.
7. I have reviewed the data illustrating CEA and PSA tissue specificity generated using the Incyte Lifeseq Gold database (Attachment II), the same database utilized to generate Example 1 in the instant application.
8. CEA is a tissue-specific marker that has been shown to be highly expressed in the GI tract. As evidenced by Attachment II, 61 out of 148 GI libraries express CEA whereas only 27 out of 1,144 other, non-GI tract libraries express this gene. Therefore, CEA is expressed approximately 17 times more in GI tissue when compared to the rest of the body.
9. Similarly, PSA is a tissue-specific marker that has been shown to be highly expressed in the prostate. As evidenced by Attachment II, 65 out of 79 prostate libraries (classified as male genitalia) express PSA whereas only 22 out of 1213 other, non-prostate libraries express this gene. Therefore, PSA is expressed approximately 45 times more in prostate when compared to the rest of the body. Further, the PSA gene product is utilized in screening, prognosis, and monitoring prostate cancer patients by oncologists and it is recommended that all men over the age of 40 be tested yearly with a PSA assay.
10. To those skilled in the art, such as myself, PSA and CEA are well known tumor markers, which indicate cancer of the prostate (PSA) and gastrointestinal (GI) tract (CEA) when the respective gene product is found in the blood sample of a patient.
11. As shown in the instant specification, (Example 1, p.55, starting on line 34) CS141 is 12 times more abundant in GI-tract tissue than non-GI tissue.
12. Clearly, CS141 is characteristic of a tissue specific marker and able to act as a cancer diagnostic, as evidenced by the above data.
13. Tissue-specific markers such as PSA and CEA are the most diagnostic tools in early oncology detection and are used on a daily basis.
14. Based on the statistics in the Incyte database, CS141 is clearly a GI specific marker and, therefore, its use as a GI tract cancer marker is unquestionable.

15. I hereby declare that all statements made herein are of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States code and such willful false statements may jeopardize the validity of the application or any patent issued thereon.


Paula N. Friedman, Ph.D.

10/10/2000
Date

ATTACHMENT I



Publications:

Wang, E.H., **Friedman, P.N.** and Prives, C. 1989. The murine p53 protein blocks replication of SV40 DNA in vitro by inhibiting the initiation functions of SV40 large T antigen. *Cell*, 57, 379-392.

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Bargonetti, J., **Friedman, P.N.**, Kern, S.E., Vogelstein, B., and Prives, C. 1991. Wild-type but not mutant p53 immunopurified proteins bind to sequences adjacent to the SV40 origin of replication. *Cell*, 65, 1083-1091.

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Bargonetti, J., Reynesdottir, I., **Friedman, P.N.**, and Prives, C. 1992. Wild-type p53 site-specific binding to cellular DNA is regulated by SV40 T antigen and mutant p53. *Genes and Devel.*, 6, 1886-1898.

Friedman, P.N., Wang, E.H., Meerovitch, K., Sonenberg, N., and Prives, C. 1992. Murine p53 inhibits the function but not the formation of SV40 T antigen hexamers and stimulates T antigen RNA helicase activity. *Chromosoma*, 102, 60-66.

Friedman, P.N., Chen, X., Bargonetti, J., and Prives, C. The p53 protein is an unusually shaped tetramer that binds directly to DNA. *PNAS*, 90, 3319-3323.

Reynesdottir, I., Lorimer, H.E., **Friedman, P.N.,** Wang, E.H., and Prives, C. 1993. Phosphorylation and active ATP hydrolysis are not required for SV40 T antigen hexamer formation. *J. of Biol. Chem.*, 268, 24647-24654.

Friedman, P.N., McAndrew, S.J., Gawlak, S.L., Chace, D., Trail, P.A., Brown, J.P., and Siegall, C.B. 1993. BR96 sFv-PE40, a potent single-chain immunotoxin that selectively kills carcinoma cells. *Cancer Res.*, 53, 334-339.

Friedman, P.N., Chace, D.F., Trail, P.A., and Siegall, C.B. 1993. Antitumor activity of the single-chain immunotoxin BR96 sFv-PE40 against established breast and lung tumor xenografts. *J. of Immun.*, 150, 3054-3061.

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